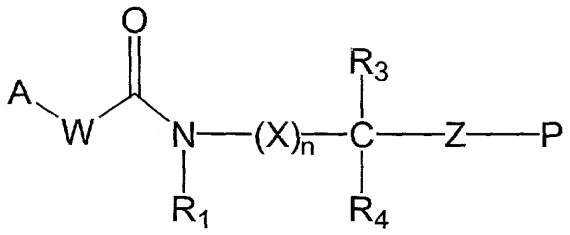
We claim:

1. A compound of Formula I,



wherein

A is a Met-AP2 inhibitory core;

W is O or $NR_2$;

$R_1$ and $R_2$ are each, independently, hydrogen or alkyl;

X is alkylene or substituted alkylene;

n is 0 or 1;

$R_3$ and $R_4$ are each, independently, hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl; or $R_3$ and $R_4$, together with the carbon atom to which they are attached, form a carbocyclic or heterocyclic group; or $R_3$ and $R_4$ together form an alkylene group;

Z is -C(O)- or alkylene-C(O)-; and

P is a peptide comprising from 1 to about 100 amino acid residues attached at its amino terminus to Z or a group $OR_5$ or $N(R_6)R_7$, wherein

$R_5$, $R_6$ and $R_7$ are each, independently, hydrogen, alkyl, substituted alkyl, azacycloalkyl or substituted azacycloalkyl; or $R_6$ and $R_7$, together with the nitrogen atom to which they are attached, form a substituted or unsubstituted heterocyclic ring structure;

or

Z is -O-, $-NR_8$-, alkylene-O- or alkylene-$NR_8$-, where $R_8$ is hydrogen or alkyl; and

P is hydrogen, alkyl or a peptide consisting of from 1 to about 100 amino acid residues attached at its carboxy terminus to Z.

2. The compound of claim 1, wherein at least one of $R_1$, $R_3$ and $R_4$ is a substituted or unsubstituted alkyl group.

3. The compound of claim 2, wherein at least one of $R_1$, $R_3$ and $R_4$ is a substituted or unsubstituted normal, branched or cyclic $C_1$-$C_6$ alkyl group.

4. The compound of claim 3, wherein at least one of $R_1$, $R_3$ and $R_4$ is a normal or branched $C_1$-$C_4$ alkyl group.

5. The compound of claim 1, wherein one of $R_3$ and $R_4$ is a substituted or unsubstituted aryl group, a substituted or unsubstituted heteroaryl group, a substituted or unsubstituted heteroarylalkyl group, or a substituted or unsubstituted aryl alkyl group.

6. The compound of claim 5, wherein one of $R_3$ and $R_4$ is selected from the group consisting of phenyl, naphthyl, indolyl, imidazolyl, pyridyl, benzyl, naphthylmethyl, indolylmethyl, imidazolylmethyl and pyridylmethyl.

7. The compound of claim 1, wherein n is 1 and X is $C_1$-$C_6$-alkylene.

8. The compound of claim 7, wherein X is methylene or ethylene.

9. The compound of claim 1, wherein Z is $C_1$-$C_6$-alkylene-C(O)-.

10. The compound of claim 9, wherein Z is methylene-C(O)- or ethylene-C(O)-.

11. The compound of claim 1, wherein at least one of $R_6$ and $R_7$ is alkyl, substituted alkyl, substituted or unsubstituted azacycloalkyl or substituted or unsubstituted azacycloalkyl.

12. The compound of claim 11, wherein at least one of $R_6$ and $R_7$ is an azacycloalkyl group having an N-alkyl substituent.

13. The compound of claim 12, wherein the N-alkyl substituent is a $C_1$-$C_4$-alkyl group.

14. The compound of claim 13, wherein the N-alkyl substituent is a methyl group.

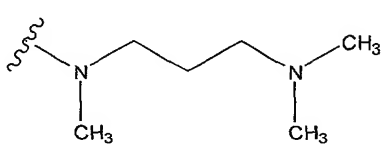
15. The compound of claim 1, wherein $R_6$ and $R_7$, together with the nitrogen atom to which they are attached, form a substituted or unsubstituted five or six-membered aza- or diazacycloalkyl group.

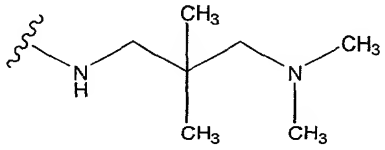
16. The compound of claim 15, wherein $R_6$ and $R_7$, together with the nitrogen atom to which they are attached, form a substituted or unsubstituted five or six-membered diazacycloalkyl group which includes an N-alkyl substituent.

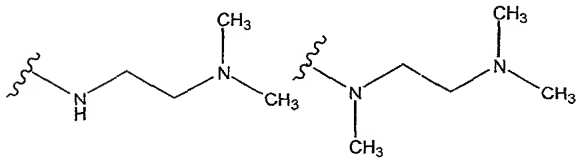
17. The compound of claim 16, wherein the N-alkyl substituent is a $C_1$-$C_4$-alkyl group.

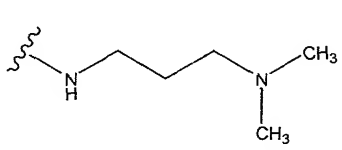
18. The compound of claim 17, wherein the N-alkyl substituent is a methyl group.

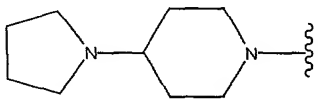
19. The compound of claim 1, wherein P is $NH_2$ or one of the groups shown below:

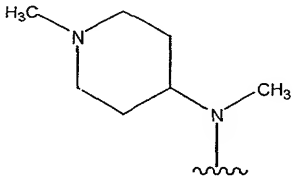


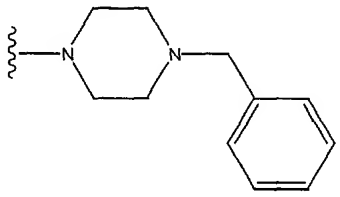


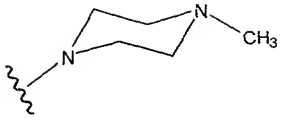


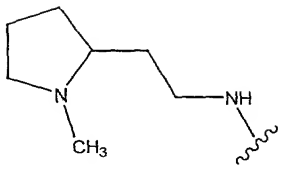




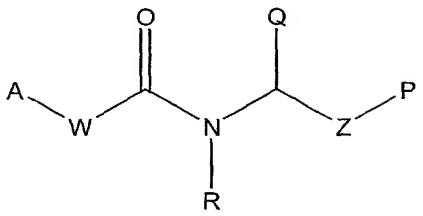







20. A compound of Formula XV,




(XV)

wherein

A is a MetAP-2 inhibitory core;

W is O or NR;

each R is, independently, hydrogen or alkyl;

Z is –C(O)- or -alkylene-C(O)-;

P is NHR, OR or a peptide consisting of one to about one hundred amino acid residues connected at the N-terminus to Z;

Q is hydrogen, linear, branched or cyclic alkyl or aryl, provided that when P is –OR, Q is not hydrogen;

or

Z is –alkylene-O- or –alkylene-N(R)-;

P is hydrogen or a peptide consisting of from one to about one hundred amino acid residues connected to Z at the carboxyl terminus;

Q is hydrogen, linear, branched or cyclic alkyl or aryl, provided that when P is hydrogen, Q is not hydrogen;

and pharmaceutically acceptable salts thereof.

21. The compound of claim 20, wherein Z is Z is –C(O)- or $C_1$-$C_4$-alkylene-C(O)-.

22. The compound of claim 21, wherein Z is -C(O)- or $C_1$-$C_2$-alkylene-C(O)-.

23. The compound of claim 21, wherein Q is linear, branched or cyclic $C_1$-$C_6$-alkyl, phenyl or naphthyl.

24. The compound of claim 23, wherein Q is isopropyl, phenyl or cyclohexyl.

25. The compound of claim 1, wherein Z is $C_1$-$C_6$-alkylene-O- or $C_1$-$C_6$-alkylene-NR-.

26. The compound of claim 25, wherein Z is $C_1$-$C_4$-alkylene-O- or $C_1$-$C_4$-alkylene-NH-.

27. The compound of claim 26, wherein Z is $C_1$-$C_2$-alkylene-O- or $C_1$-$C_2$-alkylene-NH.

28. The compound of claim 25, wherein Q is linear, branched or cyclic $C_1$-$C_6$-alkyl , phenyl or naphthyl.

29. The compound of claim 28, wherein Q is isopropyl, phenyl or cyclohexyl.

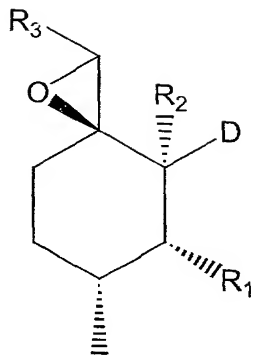
30. The compound of claim 20, wherein each R is, independently, hydrogen or linear, branched or cyclic $C_1$-$C_6$-alkyl.

31. The compound of claim 30, wherein each R is, independently, hydrogen or linear or branched $C_1$-$C_4$-alkyl.

32. The compound of claim 31, wherein each R is, independently, hydrogen or methyl.

33. The compound of claim 32, wherein each R is hydrogen.

34. The compound of claim 20, wherein A is of Formula II,




(II)

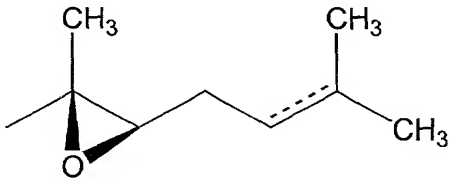
wherein

$R_1$ is hydrogen or alkoxy;

$R_2$ is hydrogen or hydroxy;

$R_3$ is hydrogen or alkyl; and

D is linear or branched alkyl or arylalkyl; or D is of the structure




35. The compound of claim 34, wherein $R_1$ is $C_1$-$C_4$-alkoxy.

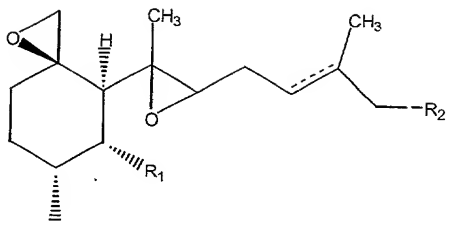
36. The compound of claim 35, wherein $R_1$ is methoxy.

37. The compound of claim 34, wherein $R_3$ is hydrogen or $C_1$-$C_4$-alkyl.

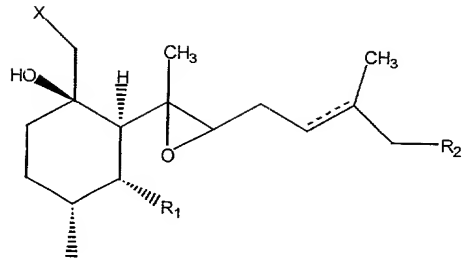
38. The compound of claim 37, wherein $R_3$ is methyl.

39. The compound of claim 34, wherein D is linear, branched or cyclic $C_1$-$C_6$-alkyl; or aryl-$C_1$-$C_4$-alkyl.

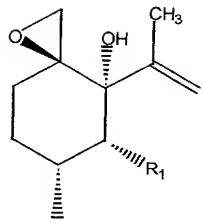
40. The compound of claim 20, wherein A is selected from the group consisting of



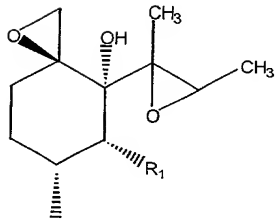
(IV)



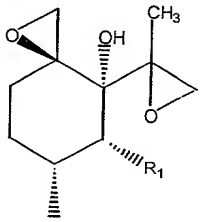
(V)



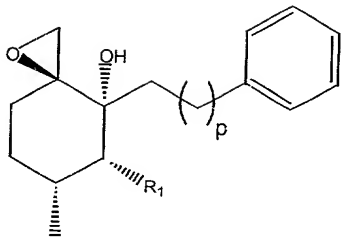
(VI)



(VII)



(VIII)



(IX)

5

Wherein

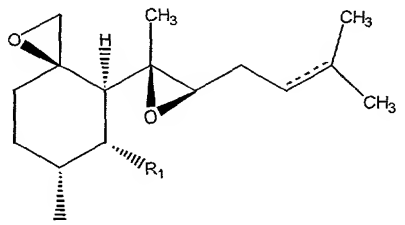
10 p is an integer from 0 to 10;

$R_1$ is hydrogen, -OH or $C_1$-$C_4$-alkoxy;

X is a leaving group; and

$R_2$ is H, OH, amino, $C_1$-$C_4$-alkylamino or di($C_1$-$C_4$-alkyl)amino).

41. The compound of claim 40, wherein A is of the formula




42. The compound of claim 20, wherein P comprises from 1 to about 20 amino acid residues.

43. The compound of claim 42, wherein P comprises an amino acid sequence which is a substrate for a matrix metalloprotease.

44. The compound of claim 43, wherein the matrix metalloprotease is selected from the group consisting of MMP-2, MMP-1, MMP-3, MMP-7, MMP-8, MMP-9, MMP-12, MMP-13 and MMP-26.

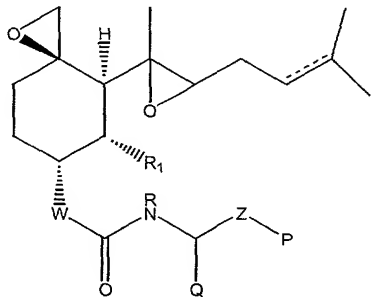
45. The compound of claim 44, wherein the matrix metalloprotease is MMP-2 or MMP-9.

46. The compound of claim 45, wherein P comprises the sequence -Pro-Leu-Gly-Xaa-, wherein Xaa is a naturally occurring amino acid residue.

47. The compound of claim 46, wherein P comprises the a sequence selected from the group consisting of Pro-Cha-Gly-Cys(Me)-His (SEQ ID NO:2); Pro-Gln-Gly-Ile-Ala-Gly-Gln-D-Arg (SEQ ID NO:3); Pro-Gln-Gly-Ile-Ala-Gly-Trp (SEQ ID NO:4); Pro-Leu-Gly-Cys(Me)-His-Ala-D-Arg (SEQ ID NO:5); Pro-Leu-Gly-Met-Trp-Ser-Arg (SEQ ID NO:35); Pro-Leu-Gly-Leu-Trp-Ala-D-Arg (SEQ ID NO:6); Pro-Leu-Ala-Leu-Trp-Ala-Arg (SEQ ID NO:7); Pro-Leu-Ala-Leu-Trp-Ala-Arg (SEQ ID NO:8); Pro-Leu-Ala-Tyr-Trp-Ala-Arg (SEQ ID NO:9); Pro-Tyr-Ala-Tyr-Trp-Met-Arg (SEQ ID NO:10); Pro-Cha-Gly-Nva-His-Ala (SEQ ID NO:11); Pro-Leu-Ala-Nva (SEQ ID NO:12); Pro-Leu-Gly-Leu (SEQ ID NO:13); Pro-Leu-Gly-Ala (SEQ ID NO:14); Arg-Pro-Leu-Ala-Leu-Trp-Arg-Ser (SEQ ID NO:15); Pro-Cha-Ala-Abu-Cys(Me)-His-Ala (SEQ ID NO:16); Pro-Cha-Ala-Gly-Cys(Me)-His-Ala (SEQ ID NO:17); Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu (SEQ ID NO:18); Pro-Lys-Pro-Leu-Ala-Leu (SEQ ID NO:19); Arg-

Pro-Lys-Pro-Tyr-Ala-Nva-Trp-Met (SEQ ID NO:20); Arg-Pro-Lys-Pro-Val-Glu-Nva-Trp-Arg (SEQ ID NO:21); Arg-Pro-Lys-Pro-Val-Glu-Nva-Trp-Arg (SEQ ID NO:22); and Arg-Pro-Lys-Pro-Leu-Ala-Nva-Trp (SEQ ID NO:23).

48. A compound of the formula



wherein

W is O or NR;

each R is, independently hydrogen or a $C_1$-$C_4$-alkyl;

Q is hydrogen; linear, branched or cyclic $C_1$-$C_6$-alkyl; or aryl;

$R_1$ is hydroxy, $C_1$-$C_4$-alkoxy or halogen;

Z is –C(O)- or $C_1$-$C_4$-alkylene;

P is NHR, OR, or a peptide comprising 1 to 100 amino acid residues attached to Z at the N-terminus; or

Z is alkylene-O or alkylene-NR; and

P is hydrogen or peptide comprising 1 to 100 amino acid residues attached to Z at the C-terminus;

or a pharmaceutically acceptable salt thereof; provided that when P is hydrogen, NHR or OR, Q is not hydrogen.

49. The compound of claim 48, wherein

W is O or NH;

Z is alkylene-O or alkylene-NH;

Q is isopropyl;

$R_1$ is methoxy; and

P comprises from 1 to 15 amino acid residues.

50. The compound of claim 49, wherein

W is O; and

P comprises 10 or fewer amino acid residues.

51. The compound of claim 48, wherein P comprises from 1 to about 20 amino acid residues.

52. The compound of claim 51, wherein P comprises an amino acid sequence which is a substrate for a matrix metalloprotease.

53. The compound of claim 52, wherein the matrix metalloprotease is selected from the group consisting of MMP-2, MMP-1, MMP-3, MMP-7, MMP-8, MMP-9, MMP-12, MMP-13 and MMP-26.

54. The compound of claim 53, wherein the matrix metalloprotease is MMP-2 or MMP-9.

55. The compound of claim 54, wherein P comprises the sequence -Pro-Leu-Gly-Xaa-, wherein Xaa is a naturally occurring amino acid residue.

56. The compound of claim 55, wherein P comprises the a sequence selected from the group consisting of Pro-Cha-Gly-Cys(Me)-His (SEQ ID NO:2); Pro-Gln-Gly-Ile-Ala-Gly-Gln-D-Arg (SEQ ID NO:3); Pro-Gln-Gly-Ile-Ala-Gly-Trp (SEQ ID NO:4); Pro-Leu-Gly-Cys(Me)-His-Ala-D-Arg (SEQ ID NO:5); Pro-Leu-Gly-Met-Trp-Ser-Arg (SEQ ID NO:35); Pro-Leu-Gly-Leu-Trp-Ala-D-Arg (SEQ ID NO:6); Pro-Leu-Ala-Leu-Trp-Ala-Arg (SEQ ID NO:7); Pro-Leu-Ala-Leu-Trp-Ala-Arg (SEQ ID NO:8); Pro-Leu-Ala-Tyr-Trp-Ala-Arg (SEQ ID NO:9); Pro-Tyr-Ala-Tyr-Trp-Met-Arg (SEQ ID NO:10); Pro-Cha-Gly-Nva-His-Ala (SEQ ID NO:11); Pro-Leu-Ala-Nva (SEQ ID NO:12); Pro-Leu-Gly-Leu (SEQ ID NO:13); Pro-Leu-Gly-Ala (SEQ ID NO:14); Arg-Pro-Leu-Ala-Leu-Trp-Arg-Ser (SEQ ID NO:15); Pro-Cha-Ala-Abu-Cys(Me)-His-Ala (SEQ ID NO:16); Pro-Cha-Ala-Gly-Cys(Me)-His-Ala (SEQ ID NO:17); Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu (SEQ ID NO:18); Pro-Lys-Pro-Leu-Ala-Leu (SEQ ID NO:19); Arg-Pro-Lys-Pro-Tyr-Ala-Nva-Trp-Met (SEQ ID NO:20); Arg-Pro-Lys-Pro-Val-Glu-Nva-Trp-Arg (SEQ ID NO:21); Arg-Pro-Lys-Pro-Val-Glu-Nva-Trp-Arg (SEQ ID NO:22); and Arg-Pro-Lys-Pro-Leu-Ala-Nva-Trp (SEQ ID NO:23).

57. An angiogenesis inhibitor compound selected from the group consisting of

{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-3-methyl-butyric acid methyl ester;

2-{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-3-methyl-butyric acid methyl ester;

2-{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-4-methyl-pentanoic acid methyl ester;

{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R* )-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-phenyl-acetic acid methyl ester;

(1-Carbamoyl-2-methyl-propyl)-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R* )-5-methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(1-Carbamoyl-2-methyl-propyl)-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R* )-5-methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(1-Hydroxymethyl-2-methyl-propyl)-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2*R*, 3*R*)- 2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

2-{(3*R*, 4*S*, 5*S*, 6*R* )-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-3,3-dimethyl-butyric acid methyl ester;

Cyclohexyl-2-{(3*R*, 4*S*, 5*S*, 6*R* )-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-acetic acid methyl ester;

2-{(3*R*, 4*S*, 5*S*, 6*R* )-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-3-methyl-pentanoic acid methyl ester;

[1-(1-Carbamoyl-2-hydroxy-ethylcarbamoyl)-2-methyl-propyl]-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R* )-5-methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl]-oxiranyl-1-oxa-spiro[2.5]oct-6-yl ester;

2-(3-{(3*R*, 4*S*, 5*S*, 6*R* )-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl}-ureido)-3-methyl-butyramide;

2-{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-3-methyl-butyric acid;

N-Carbamoyl (ID#31) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

N-Carbamoyl (ID#30) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

N-Carbamoyl (ID#32) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

N-Carbamoyl (ID#40) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

N-Carbamoyl (ID#39) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

N-Carbamoyl (ID#26) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

N-Carbamoyl (ID#27) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(ID#24)-(2*R*-{(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl} amino-3-methyl-butanol) ester;

(ID#36)-(2*R*-{(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl} amino-3-methyl-butanol) ester;

(ID#37)-(2*R*-{(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl} amino-3-methyl-butanol) ester;

(ID#38)-(2*R*-{(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl} amino-3-methyl-butanol) ester;

(ID#34)-(2*R*-{(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl} amino-3-methyl-butanol) ester;

{2-Methyl-1-[methyl-(1-methyl-piperidin-4-yl)-carbamoyl]-propyl}-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

[1-(2-Dimethylamino-ethylcarbamoyl)-2-methyl-propyl]-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

{1-[(2-Dimethylamino-ethyl)-methyl-carbamoyl]-2-methyl-propyl}-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

[1-(3-Dimethylamino-propylcarbamoyl)-2-methyl-propyl]-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

[1-(3-Dimethylamino-2,2-dimethyl-propylcarbamoyl)-2-methyl-propyl]-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

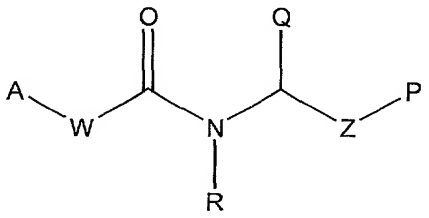
[2-Methyl-1-(4-methyl-piperazine-1-carbonyl)-propyl]-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

{2-Methyl-1-[2-(1-methyl-pyrrolidin-2-yl)-ethylcarbamoyl]-propyl}-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

[2-Methyl-1-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-propyl]-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester; and

[1-(4-Benzyl-piperazine-1-carbonyl)-2-methyl-propyl]-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester.

58. A method of treating an angiogenic disease in a subject, comprising administering to the subject a therapeutically effective amount of an angiogenesis inhibitor compound comprising the structure




(XV)

wherein

A is a MetAP-2 inhibitory core;

W is O or NR;

each R is, independently, hydrogen or alkyl;

Z is –C(O)- or -alkylene-C(O)-;

P is NHR, OR or a peptide consisting of one to about one hundred amino acid residues connected at the N-terminus to Z;

Q is hydrogen, linear, branched or cyclic alkyl or aryl, provided that when P is –OR, Q is not hydrogen;

or

Z is –alkylene-O- or –alkylene-N(R)-;

P is hydrogen or a peptide consisting of from one to about one hundred amino acid residues connected to Z at the carboxyl terminus;

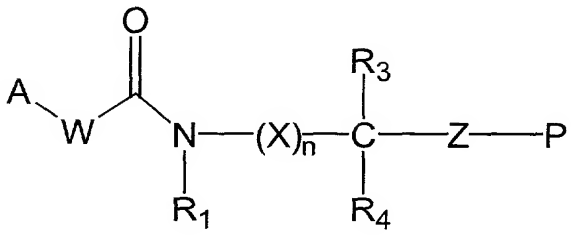
Q is hydrogen, linear, branched or cyclic alkyl or aryl, provided that when P is hydrogen, Q is not hydrogen; and a pharmaceutically acceptable salt thereof, thereby treating the angiogenic disease in the subject.

59. The method of claim 58, wherein said angiogenic disease is an autoimmune disease.

60. The method of claim 59, wherein said autoimmune disease is rheumatoid arthritis.

61. The method of claim 58, wherein said angiogenic disease is cancer.

62. A method of treating an angiogenic disease in a subject, comprising administering to the subject a therapeutically effective amount of an angiogenesis inhibitor compound comprising the structure




wherein

A is a Met-AP2 inhibitory core;

W is O or $NR_2$;

$R_1$ and $R_2$ are each, independently, hydrogen or alkyl;

X is alkylene or substituted alkylene;

n is 0 or 1;

$R_3$ and $R_4$ are each, independently, hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl; or $R_3$ and $R_4$,

together with the carbon atom to which they are attached, form a carbocyclic or heterocyclic group; or $R_3$ and $R_4$ together form an alkylene group;
Z is -C(O)- or alkylene-C(O)-; and
P is a peptide comprising from 1 to about 100 amino acid residues attached at its amino terminus to Z or a group $OR_5$ or $N(R_6)R_7$, wherein

$R_5$, $R_6$ and $R_7$ are each, independently, hydrogen, alkyl, substituted alkyl, azacycloalkyl or substituted azacycloalkyl; or $R_6$ and $R_7$, together with the nitrogen atom to which they are attached, form a substituted or unsubstituted heterocyclic ring structure;

or

Z is -O-, $-NR_8-$, alkylene-O- or alkylene-$NR_8$-, where $R_8$ is hydrogen or alkyl; and
P is hydrogen, alkyl or a peptide consisting of from 1 to about 100 amino acid residues attached at its carboxy terminus to Z.

63. The method of claim 62, wherein said angiogenic disease is an autoimmune disease.

64. The method of claim 63, wherein said autoimmune disease is rheumatoid arthritis.

65. The method of claim 62, wherein said angiogenic disease is cancer.